

REMARKS

Applicant has considered the final Office Action mailed December 23, 2008 in connection with the Application.

Disposition of the Claims

Applicant has reviewed the file history of the Application and takes this opportunity to clarify, for the record, the claim set believed to be pending. Chronologically, salient features of the prosecution history of the Application are as follows:

1. The Office issued a restriction requirement (the "First Restriction"), as set forth in a non-final action of April 16, 2007. Applicant submitted an amendment and reply thereto on August 16, 2007, which included amended claims, a provisional/proposed election (of a modified form of Group I of the First Restriction, but no election of species), and other remarks.
2. In a non-final action dated September 4, 2007, the Examiner issued substantive rejections of the claims, and also recast the form of the restriction requirement (referred to herein as the "Second Restriction"), but affirmed the prior provisional/proposed election made by the Applicant, stating that it was an "election of a species of compound of Group III" (September 4, 2007 action at page 4).
3. Applicant then submitted in response, on February 28, 2008, further claim amendments and remarks fully responsive to the rejections of record in the September 4, 2007 non-final action.
4. The Examiner, however, issued a "Supplemental Restriction/Election Requirement" (the "Third Restriction"), dated April 23, 2008, in which he stated: "[t]he claims of August 16, 2007 are being restricted and the claims submitted February 21, 2008 *[sic]* will not be entered." (April 23, 2008 Office Action at page 2 (emphasis added)).
5. Applicant responded on October 23, 2008, confirming that the "amendment and response dated February 21, 2008 *[sic]* will not be entered" (Applicant's Response at page 2) and made an election without traverse of a group and a species, in response to the Third Restriction.
6. The Examiner then issued a "Final" office action, dated December 23, 2008, designated as "Responsive to communication(s) filed on 28 February, 2008", in which the Examiner now acknowledged that the "restriction requirement was modified on 4/23/3008 *[sic]*" but that, contrary to the immediate past action and Applicant's response thereto, "[t]he claims of 2/23/2008 *[sic]* were entered with the response and amendment and are those under examination." (December 23, 2008 Office Action at page 2 (emphasis added)). The basis for the Examiner's decision to now enter the previously un-entered claim amendments and remarks of February 21, 2008 appears to be that the still further-revised restriction requirement (the "Third

Restriction”), now affirmed in the December 23, 2008 Office Action, expanded the scope of the elected group (the election having been made in response to the Second Restriction) but otherwise did not affect the substance of the rejections of record, as of September 4, 2007.

Group I of each of the three restrictions, as applied to Formula (I), are exemplified in the following Table. Mark-ups in each column show changes to the immediately preceding (left adjacent) column. The values of the variables corresponding to Applicant’s elected compound are shown in the row beneath the respective descriptions of Group I.

First (Cls. 1 – 12, 14, 15, and 18)	Second (Cls. 1, 3 – 9, 12, 18)	Third (Cls. 1, 3 – 9, 12, 18)
M^1 is CH_2 , M^2 is NR^{24} , R^1 and R^2 are H or lower alkyl, $R^3 = R^4 = R^7 = R^9 = R^8 = R^{14} = R^{15} = R^{17} = R^{24} = H$, R^6 is H or SMe, R^5 is IA, Z is O, R^{10} is cyclohexyl or phenyl, $n = 1$, $m = 0$, R^{13} is IB $p = 1$, $q = 0$, R^{16} is OH, $r = 5$.	M^1 is CH_2 , M^2 is NR^{24} , R^1 and R^2 are H or lower alkyl, $[[R^3 =]] R^4 = R^7 = R^9 = R^8 = R^{14} = R^{15} = [[R^{17} =]] R^{24} = H$, R^6 is H or SMe, R^5 is IA, Z is O, R^{10} is cyclohexyl or phenyl, $n = 1$, $m = 0$, R^{13} is IB $p = 1$, $q = 0$, R^{16} is OH, $r = 3$, R^{17} is C_{1-10} alkyl, said alkyl being ethyl and substituted with two R^{47} ’s (one on each carbon), where both R^{47} ’s are selected from hydroxyl, shown as structure I in Figure 1.	M^1 is CH_2 , M^2 is NR^{24} , R^1 and R^2 are H or lower alkyl, $R^4 = R^7 = R^9 = R^8 = R^{14} = R^{15} = R^{24} = H$, <u>one of R^5 or R^6 is H or SMe and the other is IA,</u> Z is O, R^{10} is cyclohexyl or phenyl, $n = 1$, $m = 0$, R^{13} is IB $p = 1$, $q = 0$, R^{16} is OH, $r = 3$, R^{17} is C_{1-10} alkyl, said alkyl being ethyl and substituted with two R^{47} ’s (one on each carbon), where both R^{47} ’s are selected from hydroxyl, shown as structures IA and IB in Figure 1.
<i>Elected Compound</i>	<i>Elected Compound</i> Example 1.	<i>Elected Compound</i> Example 1.

N/A	(Group I as cast does not read on Example 1)	R^1 = Ethyl R^2 = n-Butyl R^5 = H R^6 = IA R^{10} = Phenyl R^{11} = H
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Accordingly, Applicant understands the elected group to take the following form, *i.e.*,
Group I of the Third Restriction (formatting introduced herein for clarity):

Group I, drawn to compounds and compositions possessing a benzothiazepine core where in applicant's Markush structure of formula I, wherein
 M^1 is CH_2 ,
 M^2 is NR^{24} ,
 R^1 and R^2 are H or lower alkyl,
 $R^4 = R^7 = R^9 = R^8 = R^{14} = R^{15} = R^{24} = H$,
one of R^5 or R^6 is H or SMe and the other is IA,
Z is O,
 R^{10} is cyclohexyl or phenyl,
 $n=1$,
 $m=0$,
 R^{13} is IB
 $p=1$,
 $q=0$,
 R^{16} is OH,
 $r=3$,
 R^{17} is C_{1-10} alkyl, said alkyl being ethyl and substituted with two R^{47} 's (one on each carbon), where both R^{47} 's are selected from hydroxyl, shown as structures **IA** and **IB** in Figure 1 (found at page 3 of the April 23, 2008 Office Action).

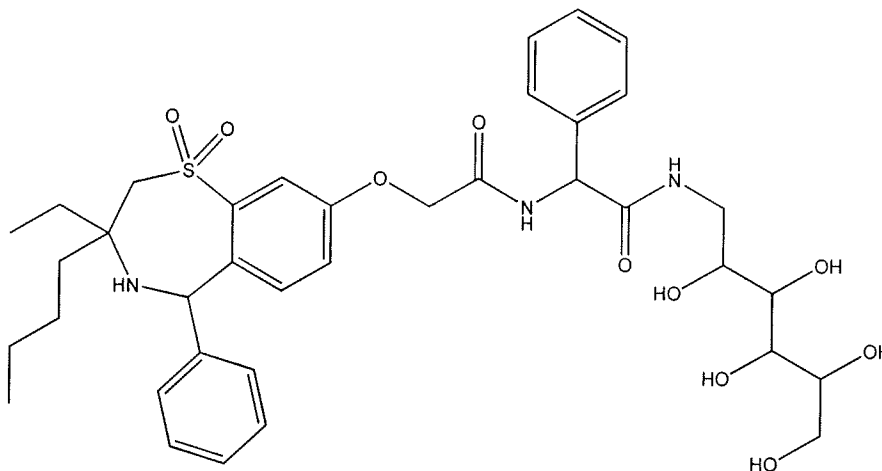
Applicant notes that this restriction group is silent as to values taken by substituent R^{11} . Furthermore Applicant notes that the two structures shown as **IA** and **IB** in the April 23, 2008 Office Action (not to be confused with the two groups IA and IB recited in Applicant's claims) differ from one another only in the values of R^5 and R^6 . This difference amounts to a difference in substitution position on the benzene ring of the benzodiazepine ring system.

According to the Examiner, pending claims 1, 4, 6, 7, 12 and 18 read on the elected group.

Applicant further understands the elected species to be the compound of Example 1, in the Application, named as:

(+/-)-trans-1,1-dioxo-3-ethyl-3-butyl-5-phenyl-7-methylthio-8-(N-{(R)- α -[N'-(2-(S)-3-(R)-4-(R)-5-(R)-2,3,4,5,6-pentahydroxylhexyl)carbamoyl]-benzyl} carbamoylmethoxy)-2,3,4,5-tetrahydro-1,4-benzothiazepine.

The elected compound (from Example 1) has the following structure:



Finally, therefore, Applicant understands the claims pending prior to entry of the instant reply to be those filed in the Application on February 28, 2008 (having now been entered), and the rejections of record to be those of the December 23, 2008 Office Action (reiterating rejections of record, applicable to claims pending as of September 4, 2007).

Amendments to Specification

Applicant amends the title of the application, to ensure that it is commensurate in scope with the subject matter of the pending claims.

Accordingly, no new matter is introduced by way of this amendment to the specification herein and entry thereof is respectfully requested.

Applicant also notes that amendments were made to the specification, in the amendment and reply dated February 28, 2008. Applicant cannot find the Examiner's acknowledgement of

these amendments in any subsequent action, and therefore is not certain that they have been entered. Applicant now asks the examiner to confirm that those amendments have in fact been entered into the file history of the Application.

Amendments to the Claims

Claims 1, 4, 6 – 7, 12 – 13, and 18 are pending in the instant Application. In the instant section, it is to be assumed that reference herein to a single portion of the specification in support of a particular amendment or new claim, is not to preclude the existence of additional support for that amendment or claim, but located elsewhere in the specification and drawings, and not specifically referenced herein.

Claims 1, 6, and 12 are amended to attend to clerical items and/or to delete certain substituents. The amendments are made, either to conform the claims to the form of the restriction requirement described herein, or to delete substituents, as is Applicant's right. An Applicant may decline to claim any material disclosed in his specification. MPEP 2173.05(i); *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187,196 (CCPA 1977) (alternative elements positively recited in the specification may be explicitly excluded from the claims).

With respect to the amendments to variables R⁵, R⁶, and R²⁰, Applicant is reinstating values recited by the claim as originally filed, but previously deleted by amendment.

Claims 4 and 7 are cancelled herein without prejudice to Applicant's rights to pursue the subject matter of the claim in one or more continuing applications that benefit of the right of priority of the instant application.

Accordingly, no new matter is introduced by way of the new claims herein and entry thereof is respectfully requested.

REJECTIONS OF THE CLAIMS

Rejections under 35 U.S.C. § 112 (¶ 2)

The Examiner has rejected claims 1, 3 – 9, 12, and 18 under 35 U.S.C. § 112 (second paragraph) as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner has objected to use of the “word [*sic*] ‘in-vitro [*sic*] hydrolysable ester or amide’ ” (Office Action at

page 5), as falling outside the subject matter of formula I and for providing “no specific structure guidance”. Applicant respectfully disagrees and traverses the rejection, as follows.

First, regarding the alleged recitation of subject matter falling outside of formula 1, Applicant sees no formalistic difference between the *in vivo* hydrolysable forms of the compounds (recited in the claims) and the pharmaceutically acceptable salts thereof. The latter term has not been objected to by the examiner.

Second, regarding the term “*in vivo* hydrolysable ester or amide”, as recited in Applicant’s claims, Applicant’s specification provides a definition and examples of how such compounds are formed and exemplary materials for forming such compounds. See, *e.g.*, page 11 of the application. These descriptions and definitions provide ample support for what is meant by the terms as well as giving explicit guidance to those skilled in the art. Applicant does not have to recite the claim to incorporate such definitions from the specification. Furthermore, Applicant believes that the definitions found at page 11 of the application are consistent with how one skilled in the art would use and understand the term.

Accordingly, Applicant respectfully requests that the rejection be withdrawn.

Rejections under 35 U.S.C. § 112 (¶ 1)

The Examiner has rejected claims 1, 4, 6 – 7, and 18 under 35 U.S.C. § 112 (first paragraph) as allegedly being non-enabled because the “specification does not reasonably provide enablement for the protracted list of compounds bearing the protracted list of substituents.” Applicant respectfully traverses the rejection.

The claims as amended herein recite lists of compounds that are considerably truncated relative to the original form of the claim. In particular, all variables hold constant value, with the exception of:

R¹ and R² (H; C₁₋₆ alkyl);

R⁵ and R⁶ (position; IA, MeS, or H);

R¹⁰: cyclohexyl or phenyl optionally substituted with R²⁸

R¹⁷: CH₂(OH)CH(OH)--, or formula IC.

R²⁰: C₁₋₁₀alkyl, optionally substituted by one or more R⁵⁷ (which can be halo or hydroxyl)

R^{28} : Halo, OH, or C_{1-10} alkoxy.

With this in mind, it can be seen both that the number of variable positions is manageable, and the number and variety of substituents to be accommodated at each position is rather conservative. Accordingly, with the amendments herein, the recited compounds no longer entail “protracted” lists of substituents to be contemplated. In particular, the literature reference used by the Examiner in support of unpredictability of properties of the various compounds is mooted by the amendments herein: the reference dwelled upon phenyl ring substituents (R_3 in the claimed formula), which have been removed from the claim by the amendments herein.

Thus, the claims as amended herein, recite groups of compounds that one skilled in the art might reasonably be able to make, based on the methods and materials described in the application specification. Applicant requests that the rejection be withdrawn.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 1, 4, 6 – 7, 12, and 18, under 35 U.S.C. § 103(a) as allegedly being obvious over WO 2003020710, (“Starke et al”). Applicant respectfully traverses the rejection based on the provisions of the 1999 American Inventors’ Protection Act that amended 35 U.S.C. § 103(c) to disqualify prior art, otherwise citable only under 35 U.S.C. §§ 102(e, f, or g), that was commonly owned as of the Application’s filing date.

Specifically, Applicant notes as follows: cited reference WO 2003/020710 to Starke *et al.*, was owned by Astrazeneca AB, has an international filing date of 30 August 2002, and published on March 13, 2003. The application timely entered the U.S. national phase, and issued as U.S. Patent No. 7,192,946 (“the ’946 patent”).

The Application, also owned by Astrazeneca AB, is a U.S. national phase application of PCT/GB04/00695, and has an international filing date of February 23, 2004.

The ’946 patent is citable under 35 U.S.C. § 102(e) by virtue of having an inventor not in common with the Application (inventor Blomberg), and an earlier effective U.S. filing date (August 30, 2002) than the Application (February 23, 2004). (cf. MPEP § 706.02(f)).

However, the ’946 patent is *not* citable under either 35 U.S.C. §§ 102(a) or 102(b) for the following reason: its earliest publication date is March 13, 2003.

The Application has an effective priority date of February 25, 2003 (GB 0304194.4). The GB priority application supports the instant claims. Therefore, the Application has an earlier priority date than the earliest publication date of the subject matter of the '946 patent.

Since the rejection of record is based on 35 U.S.C. §§ 103(a) and 102(e) only, and the cited reference (WO2003/020710) is an international application that was filed after November 29, 2000, designated the U.S., and published in the English language, that rejection is overcome because the Application and the cited reference were commonly owned as of the filing date of the Application.

Accordingly, Applicant requests that the rejection be withdrawn.

Double Patenting Rejection

The Examiner has rejected claims 1, 3 – 9, 12, and 18 on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1 – 11 of U.S. Patent No. 7,192,946. Applicant files herewith a Terminal Disclaimer under 37 C.F.R. §1.321(c), thereby addressing the rejection in full. Accordingly, withdrawal of the rejection is therefore requested.

Nevertheless, Applicant notes that a Terminal Disclaimer is being filed merely for the purpose of expediting allowance of the instant application. Applicant respectfully submits that the filing of a Terminal Disclaimer in the instant application is not to be taken as an acknowledgment of the propriety of the rejection, or an admission of obviousness of any of the instant claims over those of U.S. Patent No. 7,192,946. *See Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870 (Fed. Cir. 1991) (holding that filing of a terminal disclaimer to obviate a rejection based on nonstatutory double patenting is not an admission of the propriety of the rejection); *see also Motionless Keyboard Co. v. Microsoft Corp.*, 486 F.3d 1376, (Fed. Cir., 2007) (holding that a terminal disclaimer is not a concession of obviousness).

CONCLUSION

In view of the above remarks, Applicant respectfully submits that the subject application is in good and proper order for allowance. Withdrawal of the Examiner's rejections and early notification to this effect are earnestly solicited.

Inventor(s): Ingemar Starke et al.
Serial No. : 10/546,005
Filed : August 18, 2005
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Attorney Docket No.: 23854-0005US1

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 839-5070.

No fee is believed owed in connection with filing of this amendment and reply. However, should the Commissioner determine otherwise, the Commissioner is authorized to charge any underpayment or credit any overpayment to Fish & Richardson P.C. Deposit Account No. 06-1050 (ref. no. 23854-0005US1) for the appropriate amount.

Respectfully submitted,

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